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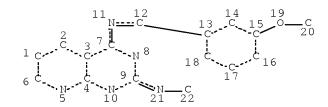
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L1 STR

L2 1 SEA SSS SAM L1

L3 37 SEA SSS FUL L1

L1 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L3 37 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 121 ITERATIONS

SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 15:12:13 ON 26 SEP 2007

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FILE COVERS 1907 - 26 Sep 2007 VOL 147 ISS 14 FILE LAST UPDATED: 25 Sep 2007 (20070925/ED)

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37 ANSWERS

L4 1 L3

=> d ibib abs hitstr

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2005:588963 CAPLUS Full-text

DOCUMENT NUMBER: 143:115560

TITLE: Preparation of pyrido[2,3-d]pyrimidine-2,4-diamines as

PDE-2 inhibitors

INVENTOR(S): Beyer, Thomas Arthur; Chambers, Robert James; Lam,

Kelvin; Li, Mei; Morrell, Andrew Ian; Thompson, David

Duane

PATENT ASSIGNEE(S): Pfizer Products Inc., USA SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	KIN	DATE			APPL	ICAT		DATE											
WO 2005061497					A1 20050707				WO 2	004-	IB40	20041206							
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,		
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,		
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,		
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NΙ,		
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,		
		ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW		
	RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	MΖ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,		
		ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,		
		EE,	ES,	FΙ,	FR,	GB,	GR,	HU,	ΙE,	IS,	IT,	LT,	LU,	MC,	NL,	PL,	PT,		
		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,		
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AU	2004	2004303609					2005	0707	AU 2004-303609						20041206				
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EP	1697	356			A1		20060906		EP 2004-801323					20041206			206		
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		BA,	HR,	IS,	YU														
	1894					A 20070110				CN 2004-80037674						20041206			
BR	2004	0176	63		Α		2007	0403		BR 2	004-	1766	3		2	0041	206		
JP	2007	5139	96		Τ		2007	0531	JP 2006-544574						2	0041	206		
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US	2007	1354	57		A1		2007				006-					0060	510		
IN	2006	DN02	850		Α		2007	0810			006-				2	0060	519		
	2006										2006-				20060615				
ИО	2006	0032	31		А		2006	0711		NO 2006-3231					20060711				
IORIT	ORITY APPLN. INFO.:										2003- 2004-					0031 0041			

GI

RN

AB Title compds. I [Z = O-alkyl; R1, R2 = H, OCH3 with provisos; n = 1-4; X = a bond, O, S, etc.; Y = benzoxazolyl, benzothiazolyl, benzofurazanyl, etc.] and their pharmaceutically acceptable salts were prepared For example, aminoarom. substitution of chloropyrimide II and 2-(2-aminoethyl)pyridine afforded pyrido[2,3-d]pyrimidine III in 40% yield. In PDE 2 inhibition assays, 4 - examples of compds. I exhibited IC50 values <50 nM.

IT 857521-01-8P 857521-02-9P 857521-03-0P 857521-04-1P 857521-05-2P 857521-06-3P 857521-07-4P 857521-08-5P 857521-09-6P 857521-10-9P 857521-11-0P 857521-12-1P 857521-13-2P 857521-14-3P 857521-15-4P 857521-16-5P 857521-17-6P 857521-18-7P 857521-19-8P 857521-20-1P 857521-22-3P 857521-22-3P 857521-23-4P 857521-23-4P 857521-23-8P 857521-23-4P 857521-23-8P 857521-23-8P 857521-23-4P 857521-23-8P 857521-23-3P 857521-33-6P 857521-33-6P 857521-34-7P 857521-35-8P 857521-36-9P 857521-37-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrido[2,3-d]pyrimidine-2,4-diamines as PDE-2 inhibitors) 857521-01-8 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)]methyl[2-(2-pyridinyl)]ethyl

RN 857521-02-9 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-<math>[2-(3-pyridinyl)ethyl]- (CA INDEX NAME)

RN 857521-03-0 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-<math>[2-(4-pyridinyl)ethyl]- (CA INDEX NAME)

RN 857521-04-1 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(3-pyridinylmethyl)- (CA INDEX NAME)

RN 857521-05-2 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N,N'-bis[(3,5-dimethoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

RN 857521-06-3 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2- [2-(4-methoxyphenyl)ethyl]- (CA INDEX NAME)

$$\begin{array}{c} \text{MeO} \\ \\ \text{CH}_2\text{--} \text{CH}_2\text{---} \text{NH} \\ \\ \text{NH} \\ \\ \text{CH}_2 \\ \\ \text{OMe} \\ \end{array}$$

RN 857521-07-4 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(3-phenylpropyl)- (CA INDEX NAME)

RN 857521-08-5 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N2-[(4-chlorophenyl)methyl]-N4-[(3,5-dimethoxyphenyl)methyl]- (CA INDEX NAME)

RN 857521-09-6 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(phenylmethyl)- (CA INDEX NAME)

RN 857521-10-9 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-[2-(2-thienyl)ethyl]- (CA INDEX NAME)

RN 857521-11-0 CAPLUS

CN Benzenemethanol, $4-[[4-[(3,5-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]methyl]-<math>\alpha$, α -dimethyl- (CA INDEX NAME)

RN 857521-12-1 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(2-phenylethyl)- (CA INDEX NAME)

RN 857521-13-2 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N2-[2-(3,5-dimethoxyphenyl)ethyl]-N4-[(3,5-dimethoxyphenyl)methyl]- (CA INDEX NAME)

RN 857521-14-3 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-[2-(3-fluorophenyl)ethyl]- (CA INDEX NAME)

$$\begin{array}{c} \text{F} \\ \text{CH}_2 \text{-CH}_2 \text{-NH} \\ \text{NH} \\ \text{CH}_2 \\ \text{OMe} \end{array}$$

RN 857521-15-4 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-[2-(2-fluorophenyl)ethyl]- (CA INDEX NAME)

RN 857521-16-5 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-[2-(4-fluorophenyl)ethyl]- (CA INDEX NAME)

RN 857521-17-6 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-(2-phenylethyl)- (CA INDEX NAME)

RN 857521-18-7 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-(4-phenylbutyl)- (CA INDEX NAME)

RN 857521-19-8 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-(2-phenoxyethyl)- (CA INDEX NAME)

RN 857521-20-1 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2- [[2-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)

RN 857521-21-2 CAPLUS

CN Benzenemethanol, $4-[2-[[4-[[(3,4-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]-<math>\alpha$, α -dimethyl- (CA INDEX NAME)

Me CH₂ - CH₂ - NH NH NH CH₂

$$\begin{array}{c} \text{MeO} \\ \text{OMe} \end{array}$$

RN 857521-22-3 CAPLUS

CN Benzenemethanol, $4-[2-[[4-[[(3,5-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]-<math>\alpha$, α -dimethyl- (CA INDEX NAME)

RN 857521-23-4 CAPLUS

CN Benzenemethanol, $4-[[4-[(3,5-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]methyl]-<math>\alpha$ -(trifluoromethyl)- (CA INDEX NAME)

RN 857521-24-5 CAPLUS

CN Ethanone, 1-[4-[3-[[4-[[(3,4-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]propyl]phenyl]- (CA INDEX NAME)

RN 857521-25-6 CAPLUS

CN Benzenemethanol, $4-[3-[[4-[[(3,4-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]propyl]-<math>\alpha$ -(trifluoromethyl)- (CA INDEX NAME)

RN 857521-26-7 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N2-[3-(2,1,3-benzoxadiazol-5-yl)propyl]-N4-[(3,4-dimethoxyphenyl)methyl]- (CA INDEX NAME)

RN 857521-27-8 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N2-[3-(6-benzothiazoly1)propy1]-N4-[(3,4-dimethoxypheny1)methy1]- (CA INDEX NAME)

RN 857521-28-9 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-[3-[3-(2-methyl-1,3-dioxolan-2-yl)phenyl]propyl]- (CA INDEX NAME)

RN 857521-29-0 CAPLUS

CN Benzenemethanol, $3-[3-[[4-[[(3,4-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]propyl]-<math>\alpha$ -methyl- (CA INDEX NAME)

RN 857521-30-3 CAPLUS

CN Benzonitrile, 4-[3-[[4-[[(3,4-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]propyl]- (CA INDEX NAME)

NC
$$(CH_2)_3 - NH$$
 NH NH CH_2 MeO OMe

RN 857521-31-4 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-[3-(4-pyridinyl)propyl]- (CA INDEX NAME)

RN 857521-32-5 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-(3-phenylpropyl)- (CA INDEX NAME)

RN 857521-33-6 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(3-phenoxypropyl)- (CA INDEX NAME)

RN 857521-34-7 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3-ethoxy-4-methoxyphenyl)methyl]- N2-(3-phenylpropyl)- (CA INDEX NAME)

RN 857521-35-8 CAPLUS

CN Benzenemethanol, $4-[3-[[4-[[(3-\text{ethoxy}-4-\text{methoxyphenyl})\text{methyl}]\text{amino}]\text{pyrido}[2,3-d]\text{pyrimidin}-2-yl]\text{amino}]\text{propyl}]-\alpha-\text{methyl}- (CA INDEX NAME)$

RN 857521-36-9 CAPLUS

CN Ethanone, 1-[4-[3-[[4-[[(3,4-dimethoxyphenyl)methyl]amino]pyrido[2,3-d]pyrimidin-2-yl]amino]propyl]phenyl]-2,2,2-trifluoro- (CA INDEX NAME)

$$F_3C$$
— C
 $(CH_2)_3$ — NH
 NH
 CH_2
 MeO
 OMe

RN 857521-37-0 CAPLUS

CN Ethanone, 1-[3-[4-[(3,4-dimethoxyphenyl)methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyl]amino]pyrido[2,3-dimethoxyphenyl]methyllmethy

d]pyrimidin-2-yl]amino]propyl]phenyl]- (CA INDEX NAME)

Ac
$$(CH_2)_{3-NH}$$
 NH CH_2 MeO OMe

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil medl, biosis, embase, caplus; s beyer t?/au; s chambers r?/au; s lam k?/au; s westerly m?/au; s morrell a?/au; s thompson d?/au

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TOTAL FOR ALL FILES

L9 761 BEYER T?/AU

L10	483	FILE	MEDLINE
L11	713	FILE	BIOSIS
L12	354	FILE	EMBASE
L13	1052	FILE	CAPLUS

TOTAL FOR ALL FILES

L14 2602 CHAMBERS R?/AU

L15	1469	FILE	MEDLINE
L16	1572	FILE	BIOSIS
L17	1315	FILE	EMBASE
L18	1264	FILE	CAPLUS

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L19 5620 LAM K?/AU
NOTE (120-124 deleted)
L25
          53 FILE MEDLINE
L26
          67 FILE BIOSIS
L27
          64 FILE EMBASE
L28
         53 FILE CAPLUS
TOTAL FOR ALL FILES
L29 237 MORRELL A?/AU
L30
        2948 FILE MEDLINE
        3971 FILE BIOSIS
L31
        2212 FILE EMBASE
L32
L33
        4092 FILE CAPLUS
TOTAL FOR ALL FILES
L34 13223 THOMPSON D?/AU
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L35 0 FILE MEDLINE
L36
           0 FILE BIOSIS
L37
L38
          0 FILE EMBASE
           1 FILE CAPLUS
TOTAL FOR ALL FILES
L39 1 L9 AND L14 AND L19 AND L29 AND L34
L40 4567 FILE MEDLINE
L41
        5087 FILE BIOSIS
L42 3613 FILE EMBASE
L43 15811 FILE CAPLUS
TOTAL FOR ALL FILES
L44 29078 LI M?/AU
=> s 144 and 139
L45 0 FILE MEDLINE
          0 FILE BIOSIS
L46
L47
          0 FILE EMBASE
L48
           1 FILE CAPLUS
TOTAL FOR ALL FILES
L49 1 L44 AND L39
=> s 149 not 14
L50
           O FILE MEDLINE
L51
L52
L53
           0 FILE BIOSIS
          0 FILE EMBASE
          0 FILE CAPLUS
TOTAL FOR ALL FILES
L54 0 L49 NOT L4
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=> fil reg;e "pyrido[2,3-d]pyrimidine-2,4-diamine"/cn 5

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STRUCTURE FILE UPDATES: 25 SEP 2007 HIGHEST RN 948051-90-9 DICTIONARY FILE UPDATES: 25 SEP 2007 HIGHEST RN 948051-90-9

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http://www.cas.org/support/stngen/stndoc/properties.html

```
E1
             1
                   PYRIDIUM, 4-STYRYL-1-VINYL-/CN
E2
                   PYRIDIUM, 4-STYRYL-1-VINYL-, P-TOLUENESULFONATE/CN
             1
             0 --> PYRIDO2, 3-DPYRIMIDINE-2, 4-DIAMINE/CN
Е3
                   PYRIDO(1''',2''':1'',2'') IMIDAZO(4'',5'':3',4') CYCLOPENTA(1'
E4
                   ,2':5,6)NAPHTH(1,2-D)AZEPIN-2(3H)-ONE, 4,5,5A,5B,6,7,7A,14,1
                   4A, 14B, 15, 16-DODECAHYDRO-5A, 7A, 10-TRIMETHYL-, (5AR-(5A.ALPHA
                   .,5BB,7AA/CN
                   PYRIDO(1''',2''':1'',2'') IMIDAZO(4'',5'':3',4') CYCLOPENTA(1'
E5
                   ,2':5,6)NAPHTH(1,2-D)AZEPIN-2(3H)-ONE, 4,5,5A,5B,6,7,7A,14,1
                   4A,14B,15,16-DODECAHYDRO-5A,7A,11-TRIMETHYL-, (5AR-(5A.ALPHA
                    .,5BB,7AA/CN
```

=> s pyrido(l)pyrimidine(l)diamine

273116 PYRIDO

619275 PYRIMIDINE

358987 DIAMINE

74 DIAMINES

358987 DIAMINE

(DIAMINE OR DIAMINES)

L60 1433 PYRIDO(L)PYRIMIDINE(L)DIAMINE

=> fil medl, biosis, embase, caplus; s 160 or pyrido(7a) pyrimidine(5a) diamine

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L61 90 FILE MEDLINE L62 156 FILE BIOSIS L63 380 FILE EMBASE L64 478 FILE CAPLUS

TOTAL FOR ALL FILES

L65 1104 L60 OR PYRIDO(7A) PYRIMIDINE(5A) DIAMINE

=> s pde2 or phosphodiesterase L66 26278 FILE MEDLINE L67 24560 FILE BIOSIS L68 26236 FILE EMBASE L69 27972 FILE CAPLUS

TOTAL FOR ALL FILES

L70 105046 PDE2 OR PHOSPHODIESTERASE

=> s 165 and 170

L71 0 FILE MEDLINE L72 0 FILE BIOSIS L73 0 FILE EMBASE L74 6 FILE CAPLUS

TOTAL FOR ALL FILES

L75 6 L65 AND L70

=> d 1-6 ibib abs hitstr

L75 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2007:173503 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 146:229376

Preparation of fused pyridofuropyrimidines as TITLE:

phosphodiesterase 4 (PDE4) inhibitors.

INVENTOR(S): Taltavull Moll, Joan; Pages Santacana, Luis Miquel PATENT ASSIGNEE(S): Almirall Prodesfarma, S. A., Spain

SOURCE: PCT Int. Appl., 61pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. WO 2007017078 A1 20070215 WO 2006-EP7218 20060721 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
            MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
             SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
             US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
                                20070916
     ES 2281251
                         Α1
                                            ES 2005-1840
                                                                   20050727
PRIORITY APPLN. INFO.:
                                            ES 2005-1840
                                                               A 20050727
OTHER SOURCE(S):
                        MARPAT 146:229376
GΙ
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Title compds. [I; G1 = CR6R7, O; R6, R7 = H, alkyl; R1, R2 = H, alkyl; R3 = (substituted) alkyl, alkoxy, amino, OH, alkylamino, dialkylamino, cycloalkylamino, aryl, heteroaryl, saturated N-bonded heterocyclyl; R4, R5 = H, alkyl, hydroxyalkyl, etc.], were prepared Thus, N5-isopropyl-2,2-dimethyl-N8-(2-morpholin-4-ylethyl)-1,2,3,4-tetrahydropyrimido[4',5':4,5]f uro[2,3-c]isoquinoline-5,8-diamine (preparation outlined) inhibited PDE4 with IC50 = 0.2 nM.

IT 925214-07-9P 925214-08-0P 925214-09-1P 925214-11-5P 925214-12-6P 925214-43-3F

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of fused pyridofuropyrimidines as PDE4 inhibitors)

RN 925214-07-9 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]furo[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,N5,2,2-tetramethyl-N8-[2-(4-morpholinyl)ethyl]-(CA INDEX NAME)

RN 925214-08-0 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]furo[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,N5,2,2-tetramethyl-N8-(3-pyridinylmethyl)- (CA INDEX NAME)

RN 925214-09-1 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]furo[3,2-d]pyrimidine-5,8-diamine, N8-[(2,3-dimethoxyphenyl)methyl]-1,4-dihydro-N5,N5,2,2-tetramethyl- (CA INDEX NAME)

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]furo[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,N5,2,2-tetramethyl-N8-[2-(4-morpholinyl)ethyl]-N8-(3-pyridinylmethyl)- (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N} \\ \text{N} \\ \text{CH}_2 \\ \text{CH}_2 \\ \text{N} \end{array}$$

RN 925214-12-6 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]furo[3,2-d]pyrimidine-5,8-diamine, N8-[(3,4-dimethoxyphenyl)methyl]-1,4-dihydro-N5,N5,2,2-tetramethyl- (CA INDEX NAME)

RN 925214-43-3 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]furo[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,2,2-trimethyl-N8-[2-(4-morpholinyl)ethyl]- (CA INDEX NAME)

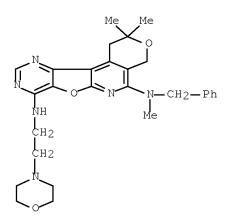
IT 925214-72-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of fused pyridofuropyrimidines as PDE4 inhibitors)

RN 925214-72-8 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]furo[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,2,2-trimethyl-N8-[2-(4-morpholinyl)ethyl]-N5-(phenylmethyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2006:542483 CAPLUS Full-text

DOCUMENT NUMBER: 145:28003

TITLE: New pyridothienopyrimidine derivatives, their

preparation and use as PDE4 inhibitors for the

treatment of pathological diseases

INVENTOR(S): Pages Santacana, Luis Miquel; Taltavull Moll, Joan;

Gracia Ferrer, Jordi

PATENT ASSIGNEE(S): Almirall Prodesfarma, S.A., Spain

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PA	TENT :	NO.			KIN	D	DATE			APPL	ICAT	DATE							
WO	2006058723				A1	_	2006	20060608		 WO 2	005-	EP12	20051130						
	W:	ΑE,	AG,	AL,	ΑM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,		
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,		
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KM,	KN,	ΚP,	KR,		
		KΖ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA,	MD,	MG,	MK,	MN,	MW,	MX,		
		MΖ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,		
		SG,	SK,	SL,	SM,	SY,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,		
		VN,	YU,	ZA,	ZM,	ZW													
	RW:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	HU,	ΙE,		
		IS,	IT,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ,		
		CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG,	BW,	GH,		
		GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,		
		KG,	KΖ,	MD,	RU,	ТJ,	TM												
ES	2259	892			A1		2006	1016		ES 2	004-	2877	20041130						
AU	2005	3114	22		A1		2006	0608		AU 2	005-	3114	20051130						
CA	2588	808			A1		2006	0608	CA 2005-2588808						20051130				
EP	1819	712			A1		2007	0822		EP 2	005-	8133	17		20051130				
	R:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	HU,	ΙE,		
		IS,	IT,	LI,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	AL,		
		BA,	HR,	MK,	YU														
PRIORIT	IORITY APPLN. INFO.:									ES 2004-2877					A 20041130				
									WO 2005-EP12773						W 20051130				
OTHER SO	THER SOURCE(S):						145:	2800	3										

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The invention is related to the use of a pyrido[3',2':4,5]thieno[3,2-AB d]pyrimidine derivative I [X = (CH2)n; n = 0-1; R1, R2 = independently H,alkyl; R3 = (un)substituted alkyl, monoalkyl/dialkyl/amino, hetero/aryl, etc.; R4, R5 = independently H, alkyl, -(CR8R9)p-A-(CR10R11)q-G2; p, q = independently 1-3; A = a bond, O, OCO , etc.; R8-R11 = independently H, alkyl; G2 = (un)substituted hetero/aryl, heterocyclyl] and their pharmaceutically acceptable salts and N-oxides, in the manufacture of a medicament for the treatment or prevention of a pathol. condition or disease susceptible to amelioration by inhibition of Phosphodiesterase 4 (PDE4). The invention is also related to the preparation of pyridothienopyrimidines I. Four pharmaceutical compns. are given. For example, II was prepared by cyclocondensation of thiopyridine III (preparation given) with 2chloroacetamide, cyclization with Et orthoformate, chlorination, and amination of chloride with 4-pyridinemethanamine. Preferred I exhibited an IC50 value < 30 nM for the inhibition of PDE4. I and their pharmaceutical compns. are useful for prevention and treatment of asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease (no data).

IT 889657-27-6P 889657-28-7P 889657-49-2P
889657-50-5P 889657-51-6P 889657-52-7P
889657-53-8P 889657-54-9P 889657-70-9P
889657-71-0P 889657-73-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of pyridothienopyrimidines as PDE4 inhibitors for treating pathol. diseases)

RN 889657-27-6 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N-(2-methoxyethyl)-N,2,2-trimethyl-N'-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 889657-28-7 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N-(2-methoxyethyl)-N,2,2-trimethyl-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)

RN 889657-49-2 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N,N,2,2-tetramethyl-N'-[2-(4-morpholinyl)ethyl]-(9CI) (CA INDEX NAME)

RN 889657-50-5 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N,N,2,2-tetramethyl-N'-[3-(4-morpholinyl)propyl]-(9CI) (CA INDEX NAME)

RN 889657-51-6 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, N8-[(2,3-dimethoxyphenyl)methyl]-1,4-dihydro-N5,N5,2,2-tetramethyl- (CA INDEX NAME)

RN 889657-52-7 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,N5,2,2-tetramethyl-N8-(4-pyridinylmethyl)- (CA INDEX NAME)

RN 889657-53-8 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,N5,2,2-tetramethyl-N8-(3-pyridinylmethyl)- (CA INDEX NAME)

RN 889657-54-9 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,N5,2,2-tetramethyl-N8-(2-pyridinylmethyl)- (CA INDEX NAME)

RN 889657-70-9 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,2,2-trimethyl-N8-[2-(4-morpholinyl)ethyl]- (CA INDEX NAME)

RN 889657-71-0 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N5,2,2-trimethyl-N8-(3-pyridinylmethyl)- (CA INDEX NAME)

RN 889657-73-2 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-

diamine, 1,4-dihydro-N5,2,2-trimethyl-N8-[2-(4-morpholinyl)ethyl]-N8-(3-pyridinylmethyl)- (CA INDEX NAME)

IT 889656-87-5P 889656-88-6P 889656-90-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of pyridothienopyrimidines as PDE4 inhibitors

for

treating pathol. diseases)

RN 889656-87-5 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N,2,2-trimethyl-N'-[2-(4-morpholinyl)ethyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

RN 889656-88-6 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N,2,2-trimethyl-N-(phenylmethyl)-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)

RN 889656-90-0 CAPLUS

CN 2H-Pyrano[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-5,8-diamine, 1,4-dihydro-N,2,2-trimethyl-N'-[2-(4-morpholinyl)ethyl]-N-(phenylmethyl)-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} & \text{Me} \\ \text{O} \\ \text{N} \\ \text{CH}_2 \\ \text{CH}_2 \\ \text{N} \end{array}$$

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2006:539368 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 145:46072

TITLE: New pyridothienopyrimidine derivatives, their

preparation and use as PDE4 inhibitors for the

treatment of pathological diseases

INVENTOR(S): Pages Santacana, Lluis Miquel; Taltavull Moll, Joan

PATENT ASSIGNEE(S): Almirall Prodesfarma, S.A., Spain

SOURCE: PCT Int. Appl., 121 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT N	KIN	D	DATE			APPLICATION NO.						DATE				
WO 20060		A1	A1 20060608			,	WO 2	005-		20051130						
W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KN,	KP,	KR,

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KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
                                20061016
                                           ES 2004-2876
                                                                   20041130
     ES 2259891
                         Α1
     AU 2005311423
                                20060608
                                           AU 2005-311423
                         Α1
                                                                   20051130
     CA 2588741
                         Α1
                                20060608
                                           CA 2005-2588741
                                                                   20051130
     EP 1819710
                         Α1
                                20070822
                                           EP 2005-814833
                                                                   20051130
         R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
             BA, HR, MK, YU
                                20070831
     IN 2007DN03938
                         Α
                                            IN 2007-DN3938
                                                                   20070525
PRIORITY APPLN. INFO.:
                                            ES 2004-2876
                                                                A 20041130
                                                               W 20051130
                                            WO 2005-EP12774
OTHER SOURCE(S):
                       MARPAT 145:46072
GΙ
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The invention is related to the use of a pyridothienopyrimidine derivative I AΒ [X = (G1)m; G1 = CR6R7, NR6; R6, R7 = independently H, alkyl; Y = (CH2)n; m, n= independently 0-1; R1, R2 = independently H , alkyl; R3 = (un)substituted alkyl, monoalkyl/dialkyl/amino, hetero/aryl, etc.; R4, R5 = independently H, alkyl, -(CR8R9)p-A-(CR10R11)q-G2; p, q = independently 1-3; A = a bond, O, OCO , etc.; R8-R11 = independently H, alkyl; G2 = (un)substituted hetero/aryl, heterocyclyl], and their pharmaceutically acceptable salts and N-oxides, in the manufacture of a medicament for the treatment or prevention of a pathol. condition or disease susceptible to amelioration by inhibition of Phosphodiesterase 4 (PDE4). The invention is also related to the preparation of pyridothienopyrimidines I. Four pharmaceutical compns. are given. For example, II was prepared by cyclocondensation of thiopyridine III with 2chloroacetamide, cyclization with Et orthoformate, chlorination, and amination of the chloride with [2-(morpholin-4-yl)ethyl]amine. Preferred I exhibited an IC50 value < 30 nM for the inhibition of PDE4. I and their pharmaceutical compns. are useful for prevention and treatment of asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease (no data).

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IT 890024-43-8P 890024-44-9P 890024-46-1P 890024-48-3P 890024-49-4P 890024-52-9P 890024-53-0P 890024-54-1P 890024-64-3P 890024-66-5P 890024-68-7P 890024-71-2P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

RN 890024-43-8 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, 2,3-dihydro-N4,N4,2,2-tetramethyl-N7-[2-(4-morpholinyl)ethyl]- (CA INDEX NAME)

RN 890024-44-9 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, 2,3-dihydro-N4,N4,2,2-tetramethyl-N7-(3-pyridinylmethyl)- (CA INDEX NAME)

RN 890024-46-1 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, N7-(2-furanylmethyl)-2,3-dihydro-N4,N4,2,2-tetramethyl- (CA INDEX NAME)

RN 890024-48-3 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, 2,3-dihydro-N4,N4,1,1-tetramethyl-N7-[2-(4-morpholinyl)ethyl]- (CA INDEX NAME)

RN 890024-49-4 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, 2,3-dihydro-N4,N4,1,1-tetramethyl-N7-(3-pyridinylmethyl)- (CA INDEX NAME)

RN 890024-52-9 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, 2,3-dihydro-N7-[2-(1H-imidazol-4-yl)ethyl]-N4,N4,1,1-tetramethyl- (9CI) (CA INDEX NAME)

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, N7-(2-furanylmethyl)-2,3-dihydro-N4,N4,1,1-tetramethyl- (CA INDEX NAME)

RN 890024-54-1 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, N7-[(2,3-dimethoxyphenyl)methyl]-2,3-dihydro-N4,N4,1,1-tetramethyl- (CA INDEX NAME)

RN 890024-64-3 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, N-ethyl-2,3-dihydro-N,2,2-trimethyl-N'-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 890024-66-5 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, N-ethyl-2,3-dihydro-N,2,2-trimethyl-N'-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)

RN 890024-68-7 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, N'-[(2,3-dimethoxyphenyl)methyl]-N-ethyl-2,3-dihydro-N,2,2-trimethyl-(9CI) (CA INDEX NAME)

RN 890024-71-2 CAPLUS

CN 1H-Cyclopenta[4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine-4,7-diamine, N4-ethyl-2,3-dihydro-N4,2,2-trimethyl-N7-[2-(4-morpholinyl)ethyl]-N7-(3-pyridinylmethyl)- (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2005:588963 CAPLUS Full-text

DOCUMENT NUMBER: 143:115560

TITLE: Preparation of pyrido[2,3-d]

pyrimidine-2,4-diamines as PDE-2

inhibitors

INVENTOR(S): Beyer, Thomas Arthur; Chambers, Robert James; Lam,

Kelvin; Li, Mei; Morrell, Andrew Ian; Thompson, David

Duane

PATENT ASSIGNEE(S): Pfizer Products Inc., USA SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.					KIN	D _	DATE		APPLICATION NO.						DATE			
WO	2005	0614	97		A1		2005	0707	WO 2004-IB4013						20041206			
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	
		AZ,	BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IS,	ΙT,	LT,	LU,	MC,	NL,	PL,	PT,	
		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	
		MR,	NE,	SN,	TD,	ΤG												
ΑU	2004	3036	09		A1		2005	0707		AU 2	004-		20041206					
CA	2549	510			A1		2005	0707	CA 2004-2549510						20041206			
EP	1697	356			A1		2006	0906	EP 2004-801323						20041206			
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,	
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BR	2004	0176	63		А		2007	0403		BR 2	004-	1766	3		2	0041	206	
JP	2007	5139	96		Τ		2007	0531		JP 2	006-	5445	74		20041206			
$N\Gamma$	1027	787			A1		2005	0621		NL 2	004-	1027	787		20041215			
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US 2007135457	A1	20070614	US	2006-595766		20060510
IN 2006DN02850	A	20070810	IN	2006-DN2850		20060519
MX 2006PA06777	A	20060823	MX	2006-PA6777		20060615
NO 2006003231	A	20060711	NO	2006-3231		20060711
PRIORITY APPLN. INFO.:			US	2003-529994P	P	20031216
			WO	2004-IB4013	W	20041206

GΙ

Title compds. I [Z = O-alkyl; R1, R2 = H, OCH3 with provisos; n = 1-4; X = a bond, O, S, etc.; Y = benzoxazolyl, benzothiazolyl, benzofurazanyl, etc.] and their pharmaceutically acceptable salts were prepared For example, aminoarom. substitution of chloropyrimide II and 2-(2-aminoethyl)pyridine afforded pyrido[2,3-d]pyrimidine III in 40% yield. In PDE 2 inhibition assays, 4 - examples of compds. I exhibited IC50 values <50 nM.

IT 857521-01-8P 857521-02-9P 857521-03-0P 857521-04-1P 857521-05-2P 857521-06-3P 857521-07-4P 857521-08-5P 857521-09-6P 857521-10-9P 857521-12-1P 857521-13-2P 857521-14-3P 857521-15-4P 857521-16-5P 857521-17-6P 857521-18-7P 857521-19-8P 857521-20-1P 857521-26-7P 857521-27-8P 857521-28-9P 857521-33-6P 857521-34-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrido[2,3-d]pyrimidine-2,4-diamines as PDE-2 inhibitors)

RN 857521-01-8 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-[2-(2-pyridinyl)ethyl]- (CA INDEX NAME)

RN 857521-02-9 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-<math>[2-(3-pyridinyl)ethyl]- (CA INDEX NAME)

RN 857521-03-0 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)]methyl[2-(4-pyridinyl)]ethyl[-(CA INDEX NAME)]

RN 857521-04-1 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(3-pyridinylmethyl)- (CA INDEX NAME)

RN 857521-05-2 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N,N'-bis[(3,5-dimethoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

RN 857521-06-3 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-[2-(4-methoxyphenyl)ethyl]- (CA INDEX NAME)

$$\begin{array}{c} \text{MeO} \\ \\ \text{CH}_2 \\ \text{CH}_2 \\ \\ \text{MeO} \\ \end{array} \\ \begin{array}{c} \text{N} \\ \text{N} \\ \text{NH} \\ \text{CH}_2 \\ \\ \text{OMe} \\ \end{array}$$

RN 857521-07-4 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(3-phenylpropyl)- (CA INDEX NAME)

RN 857521-08-5 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N2-[(4-chlorophenyl)methyl]-N4-[(3,5-dimethoxyphenyl)methyl]- (CA INDEX NAME)

RN 857521-09-6 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(phenylmethyl)- (CA INDEX NAME)

RN 857521-10-9 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-[2-(2-thienyl)ethyl]- (CA INDEX NAME)

RN 857521-12-1 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(2-phenylethyl)- (CA INDEX NAME)

RN 857521-13-2 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N2-[2-(3,5-dimethoxyphenyl)ethyl]-N4-[(3,5-dimethoxyphenyl)methyl]- (CA INDEX NAME)

RN 857521-14-3 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-[2-(3-fluorophenyl)ethyl]- (CA INDEX NAME)

F
$$CH_2-CH_2-NH$$
 NH CH_2 MeO OMe

RN 857521-15-4 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-[2-(2-fluorophenyl)ethyl]- (CA INDEX NAME)

RN 857521-16-5 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-[2-(4-fluorophenyl)ethyl]- (CA INDEX NAME)

RN 857521-17-6 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-(2-phenylethyl)- (CA INDEX NAME)

RN 857521-18-7 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-(4-phenylbutyl)- (CA INDEX NAME)

RN 857521-19-8 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-(2-phenoxyethyl)- (CA INDEX NAME)

RN 857521-20-1 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2- [[2-(trifluoromethyl)phenyl]methyl]- (CA INDEX NAME)

RN 857521-26-7 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N2-[3-(2,1,3-benzoxadiazol-5-yl)propyl]-N4-[(3,4-dimethoxyphenyl)methyl]- (CA INDEX NAME)

RN 857521-27-8 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N2-[3-(6-benzothiazoly1)propy1]-N4[(3,4-dimethoxypheny1)methy1]- (CA INDEX NAME)

RN 857521-28-9 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-[3-[3-(2-methyl-1,3-dioxolan-2-yl)phenyl]propyl]- (CA INDEX NAME)

RN 857521-31-4 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-[3-(4-pyridinyl)propyl]- (CA INDEX NAME)

RN 857521-32-5 CAPLUS

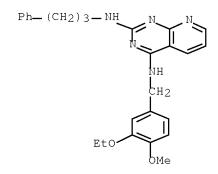
CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,4-dimethoxyphenyl)methyl]-N2-(3-phenylpropyl)- (CA INDEX NAME)

RN 857521-33-6 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3,5-dimethoxyphenyl)methyl]-N2-(3-phenoxypropyl)- (CA INDEX NAME)

RN 857521-34-7 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine, N4-[(3-ethoxy-4-methoxyphenyl)methyl]- N2-(3-phenylpropyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:563288 CAPLUS Full-text

DOCUMENT NUMBER: 139:307967

TITLE: New Base Pairing Motifs. The Synthesis and Thermal

Stability of Oligodeoxynucleotides Containing

Imidazopyridopyrimidine Nucleosides with the Ability

to Form Four Hydrogen Bonds

AUTHOR(S): Minakawa, Noriaki; Kojima, Naoshi; Hikishima, Sadao;

Sasaki, Takashi; Kiyosue, Arihiro; Atsumi, Naoko;

Ueno, Yoshihito; Matsuda, Akira

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Hokkaido

University, Sapporo, 060-0812, Japan

SOURCE: Journal of the American Chemical Society (2003),

125(33), 9970-9982

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:307967

The synthesis and thermal stability of oligodeoxynucleotides (ODNs) containing imidazo[5',4':4,5]pyrido[2,3-d]pyrimidine nucleosides 1-4 (NN, OO, NO, and ON, resp.) with the aim of developing two sets of new base pairing motifs consisting of four hydrogen bonds (H-bonds) is described. The proposed four tricyclic nucleosides were synthesized through the Stille coupling reaction of a 5-iodoimidazole nucleoside with an appropriate 5-stannylpyrimidine derivative, followed by an intramol. cyclization. These nucleosides were

incorporated into ODNs to investigate the H-bonding ability. When one mol. of the tricyclic nucleosides was incorporated into the center of each 17mer ODNs, no apparent specificity of base pairing was observed, and all duplexes were less stable than the duplexes containing natural G:C and A:T pairs. On the other hand, when three mols. of the tricyclic nucleosides were consecutively incorporated into the center of each 17mer ODNs, thermal and thermodn. stabilization of the duplexes due to the specific base pairings was observed The melting temperature (Tm) of the duplex containing the NO:ON pairs showed the highest Tm of 84.0 °C, which was 18.2 and 23.5 °C higher than that of the duplexes containing G:C and A:T pairs, resp. This result implies that NO and ON form base pairs with four H-bonds when they are incorporated into ODNs. The duplex containing NO:ON pairs was markedly stabilized by the assistance of the stacking ability of the imidazopyridopyrimidine bases. Thus, we developed a thermally stable new base pairing motif, which should be useful for the stabilization and regulation of a variety of DNA structures.

IT 597551-46-7P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (synthesis and thermal stability of oligodeoxyribonucleotides containing imidazopyridopyrimidine nucleosides with ability to form four hydrogen bonds)

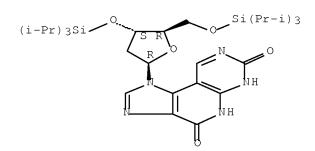
RN 597551-46-7 CAPLUS

CN 1H-Imidazo[4',5':4,5]pyrido[2,3-d]pyrimidine-4,7(5H,6H)-dione, $1-[2-\text{deoxy-3,5-bis-O-[tris(1-\text{methylethyl})silyl]-}\beta-\text{D-erythro-}$ pentofuranosyl]-, compd. with 1-[2-deoxy-3,5-bis-O-[tris(1-methylethyl)silyl]- β -D-erythro-pentofuranosyl]-1H-imidazo[4',5':4,5]pyrido[2,3-d]pyrimidine-4,7-diamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 597551-36-5 CMF C31 H53 N5 O5 Si2

Absolute stereochemistry.



CM 2

CRN 597551-28-5 CMF C31 H55 N7 O3 Si2

Absolute stereochemistry.

IT 597551-28-5P 597551-30-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and thermal stability of oligodeoxyribonucleotides containing imidazopyridopyrimidine nucleosides with ability to form four hydrogen bonds)

RN 597551-28-5 CAPLUS

CN 1H-Imidazo[4',5':4,5]pyrido[2,3-d]pyrimidine-4,7-diamine, $1-[2-\text{deoxy-3,5-bis-O-[tris(1-\text{methylethyl})silyl]-}\beta-\text{D-erythro-pentofuranosyl}]- (9CI) (CA INDEX NAME)$

Absolute stereochemistry.

RN 597551-30-9 CAPLUS

CN 1H-Imidazo[4',5':4,5]pyrido[2,3-d]pyrimidine-4,7-diamine, $1-(2-deoxy-\beta-D-erythro-pentofuranosyl)-$ (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1994:124400 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 120:124400

TITLE: Chemical synthesis of new pyridine derivatives acting

as inhibitors of phosphodiesterase

AUTHOR(S): Pallas, M.; Jimenez, A.; Victory, P.; Borrell, J. I.;

Vidal-Ferran, A.; Escubedo, E.; Camarasa, J.

CORPORATE SOURCE: Fac. Pharm., Univ. Barcelona, Barcelona, E-08028,

Spain

SOURCE: Pharmaceutical and Pharmacological Letters (1993),

3(1), 36-9

CODEN: PPLEE3; ISSN: 0939-9488

DOCUMENT TYPE: Journal LANGUAGE: English

GΙ

AB The chemical synthesis of new pyridine derivs, and their pharmacol, activity as inhibitors of phosphodiesterase are reported. Among them IQS-4 was the most potent inhibitor (IC50 5.8 $\mu\text{M})$ and this effect has a good correlation with a relaxant effect on carbachol-contracted guinea-pig trachea (IC50 73.4 $\mu\text{M})$. A preferential effect of these compds, on phosphodiesterase type IV was deduced are reported.

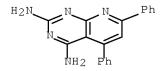
IT 20732-44-9P, IQS 2

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and phosphodiesterase inhibitory activity of)

RN 20732-44-9 CAPLUS

CN Pyrido[2,3-d]pyrimidine-2,4-diamine,5,7-diphenyl-(9CI) (CA INDEX NAME)



=> dis his nofile

(FILE 'HOME' ENTERED AT 15:09:41 ON 26 SEP 2007)

FILE 'REGISTRY' ENTERED AT 15:09:49 ON 26 SEP 2007

L1 STR

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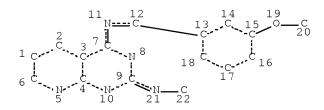
L3 37 SEA SSS FUL L1

D L3 QUE STAT

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TOTAL FOR ALL FILES
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L32
L33
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L37
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L60
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L62
L63
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L72
L73
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=> d 13 que stat;d 160 que stat L1 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 121 ITERATIONS 37 ANSWERS

SEARCH TIME: 00.00.01

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=> log y

STN INTERNATIONAL LOGOFF AT 15:18:11 ON 26 SEP 2007